#5

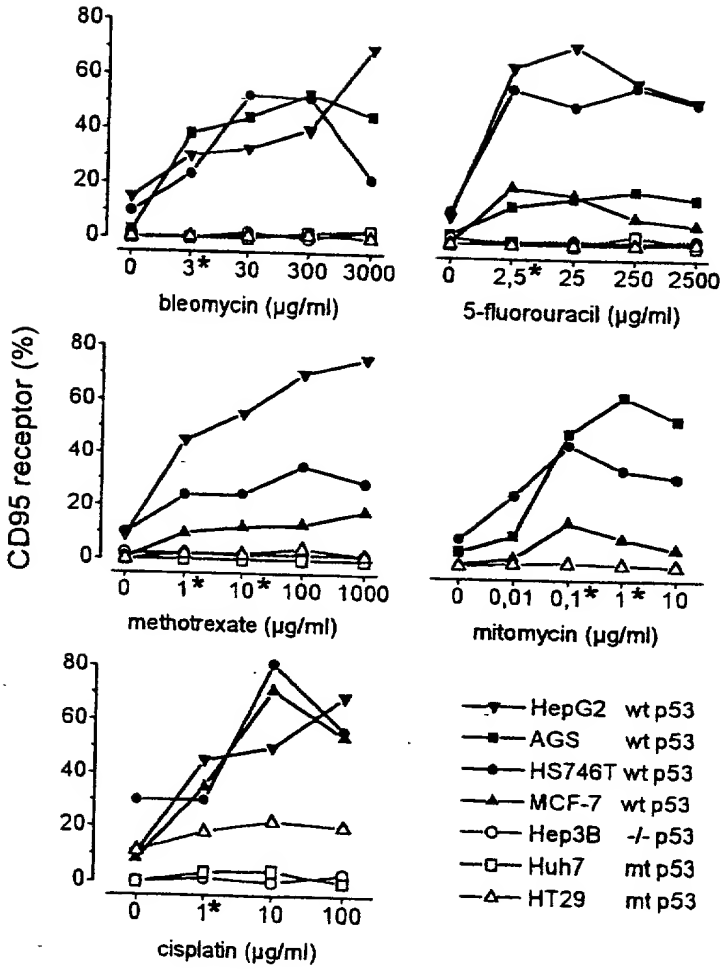

CD95 receptor (%)
80
60
40
20
0
0 3* 30 300 3000
bleomycin (µg/ml)
0 2,5* 25 250 2500
5-fluorouracil (µg/ml)
0 1* 10* 100 1000
methotrexate (µg/ml)
0 0,01 0,1* 1* 10
mitomycin (µg/ml)
0 1* 10 100
cisplatin (µg/ml)
HepG2 wt p53
AGS wt p53
HS746T wt p53
MCF-7 wt p53
Hep3B -/- p53
Huh7 mt p53
HT29 mt p53

Fig. 1

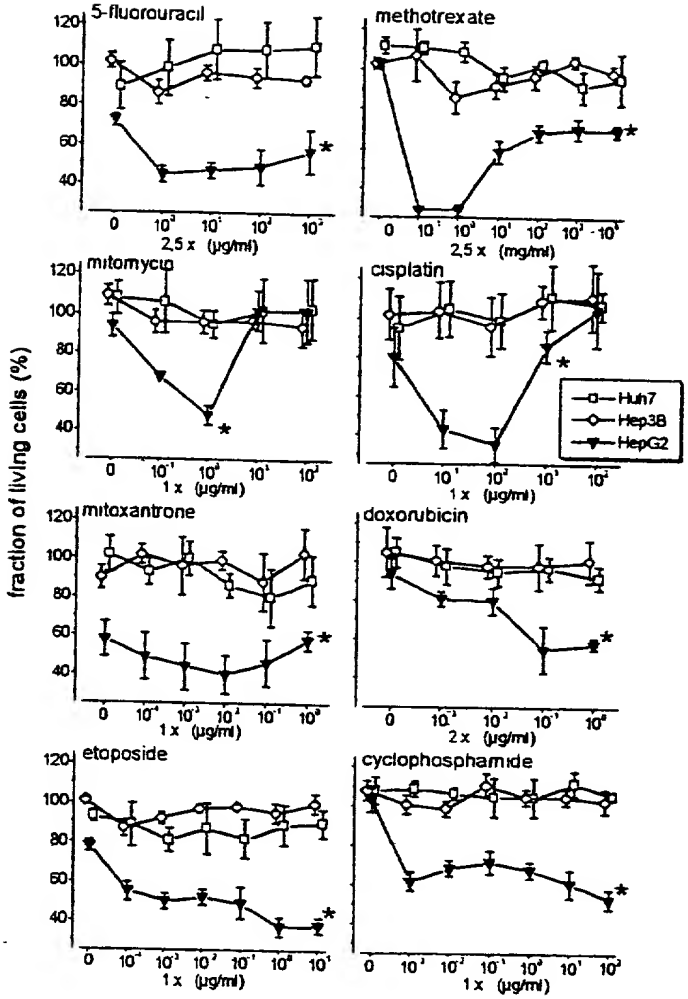


Fig. 2

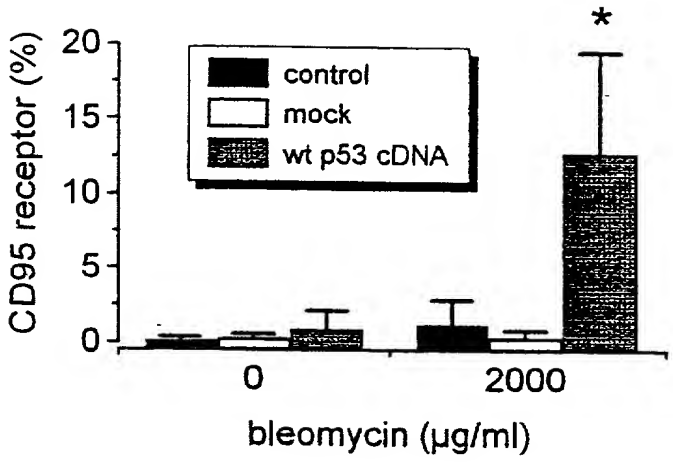

CD95 receptor (%)
20
15
10
5
0
control
mock
wt p53 cDNA
*
0
2000
bleomycin (µg/ml)

Fig. 3

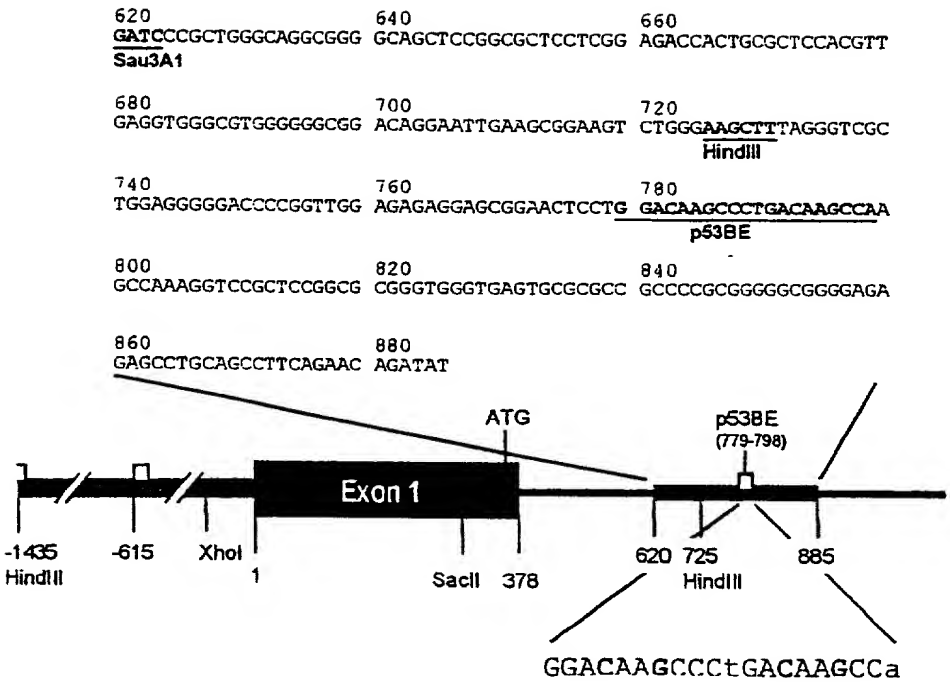
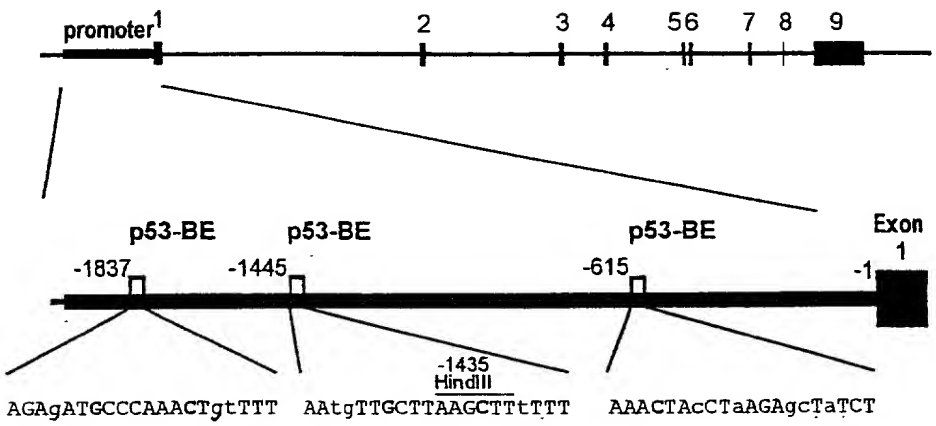


Fig. 4


promoter
1
2
3
4
56
7
8
9
p53-BE
p53-BE
p53-BE
Exon
1
-1837
-1445
-615
-1
-1435
HindIII
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AAtgTTGCTTAAGCTTtTTT
AAACTAcCTaAGAgcTaTCT

Fig. 5

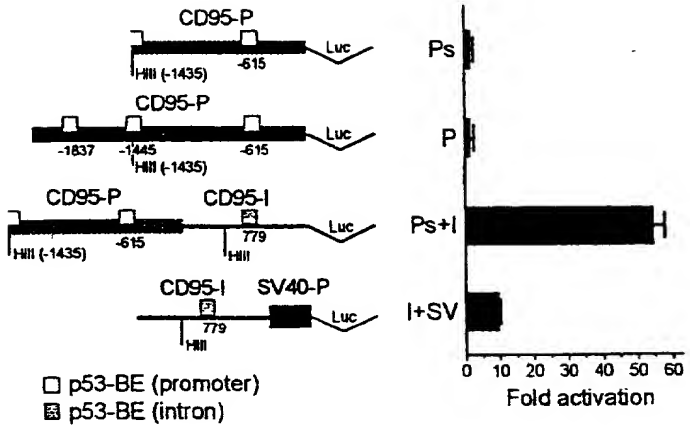
CD95-P
Luc
HIII (-1435)
-615
CD95-P
-1837
-1445
HIII (-1435)
-615
Luc
CD95-P
CD95-I
-615
779
HIII (-1435)
HIII
Luc
CD95-I
SV40-P
779
HIII
Luc
p53-BE (promoter)
p53-BE (intron)
Ps
P
Ps+I
I+SV
0 10 20 30 40 50 60
Fold activation

Fig. 6

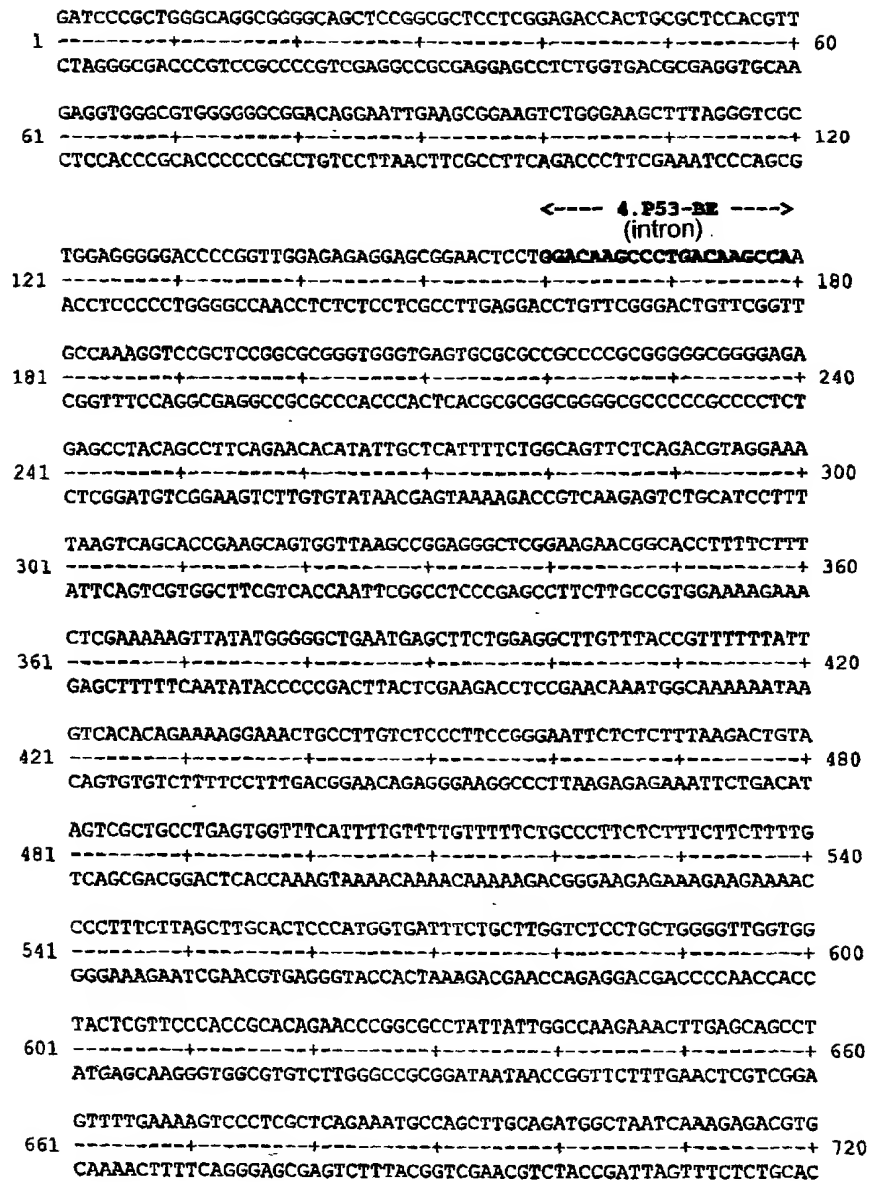

Fig. 7

2nd half of the
2.p53-BE
(promoter)

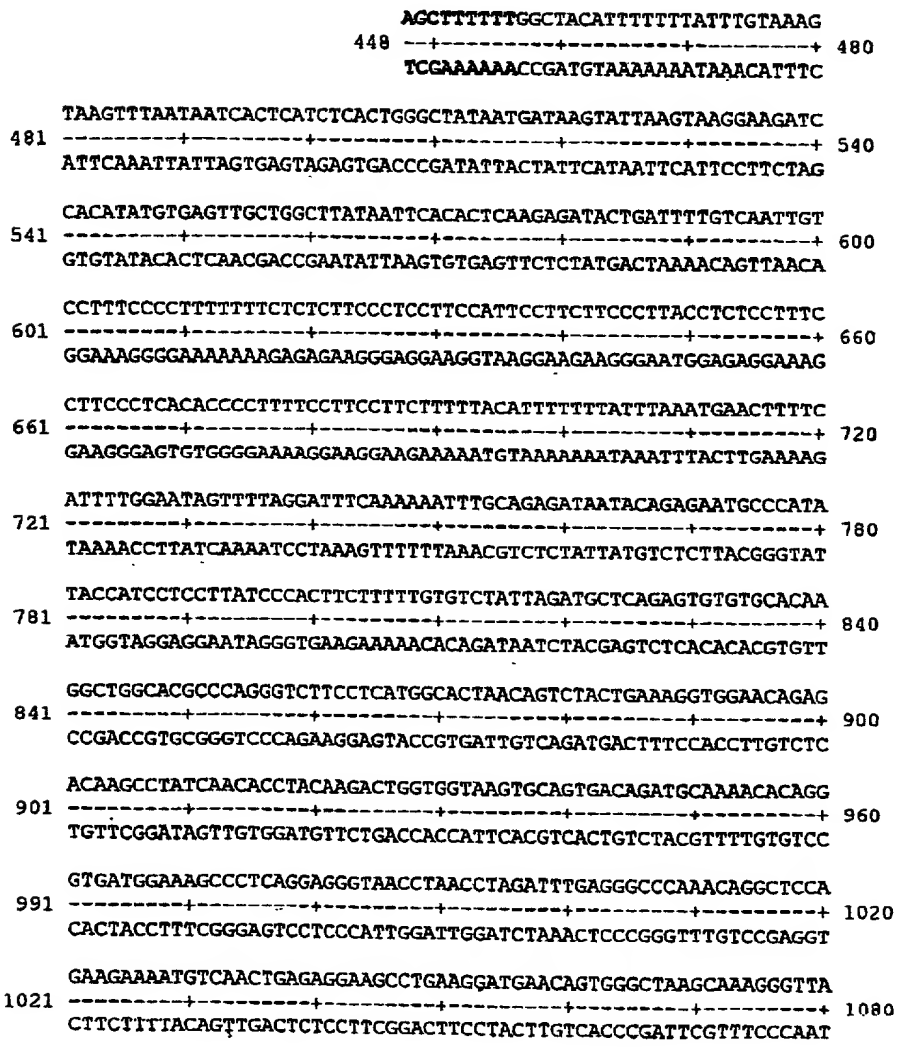

Fig. 8A

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       GCAGAGCTTGGTGGACGATGCCAAAGGAATACTGAAACCTTTAGTGTGTCCAGTCTGGAA
  1141 ---------+---------+---------+---------+---------+---------+ 1200
       CGTCTCGAACCACCTGCTACGGTTTCCTTATGACTTTGGAAATCACACAGGTCAGACCTT

       CTGCATCCAAATTCAGGTTCAGTAATGATGTCATTATCCAAACATACCTTCTGTAAAATT
  1201 ---------+---------+---------+---------+---------+---------+ 1260
       GACGTAGGTTTAAGTCCAAGTCATTACTACAGTAATAGGTTTGTATGGAAGACATTTTAA

            ←--- 3.p53-BE ----→
                (promoter)

       CATGCTAAACTACCTAAGAGCTATCTACCGTTCCAAAGCAATAGTGACTTTGAACAGTGT
  1261 ---------+---------+---------+---------+---------+---------+ 1320
       GTACGATTTGATGGATTCTCGATAGATGGCAAGGTTTCGTTATCACTGAAACTTGTCACA

       TCACCAGAGCACGAAAGAATTACAAGATTTTTTTTAAAGAAAATTGGCCAGGAAATAAT
  1321 ---------+---------+---------+---------+---------+---------+ 1380
       AGTGGTCTCGTGCTTTCTTAATGTTCTAAAAAAAATTTCTTTTAACCGGTCCTTTATTA

       GAGTAACGAAGGACAGGAAGTAATTGTGAATGTTTAATATAGCTGGGGCTATGCGATTTG
  1381 ---------+---------+---------+---------+---------+---------+ 1440
       CTCATTGCTTCCTGTCCTTCATTAACACTTACAAATTATATCGACCCCGATACGCTAAAC

       GCTTAAGTTGTTAGCTTTGTTTTCCTCTTGAGAAATAAAAACTAAGGGGCCCTCCCTTTT
  1441 ---------+---------+---------+---------+---------+---------+ 1500
       CGAATTCAACAATCGAAACAAAAGGAGAACTCTTTATTTTTGATTCCCCGGGAGGGAAAA

       CAGAGCCCTATGGCGCAACATCTGTACTTTTTCATATGGTTAACTGTCCATTCCAGGAAC
  1501 ---------+---------+---------+---------+---------+---------+ 1560
       GTCTCGGGATACCGCGTTGTAGACATGAAAAAGTATACCAATTGACAGGTAAGGTCCTTG

       GTCTGTGAGCCTCTCATGTTGCAGCCACAACATGGACAGCCCAGTCAAATGCCCCGCAAG
  1561 ---------+---------+---------+---------+---------+---------+ 1620
       CAGACACTCGGAGAGTACAACGTCGGTGTTGTACCTGTCGGGTCAGTTTACGGGGCGTTC

       TCTTTCTCTGAGTGACTCCAGCAATTAGCCAAGGCTCCTGTACCCAGGCAGGACCTCTGC
  1621 ---------+---------+---------+---------+---------+---------+ 1680
       AGAAAGAGACTCACTGAGGTCGTTAATCGGTTCCGAGGACATGGGTCCGTCCTGGAGACG

       GCTCTGAGCTCCATTCTCCTTCAAGACCTCCCCAACTTCCCAGGTTGAACTACAGCAGAA
  1681 ---------+---------+---------+---------+---------+---------+ 1740
       CGAGACTCGAGGTAAGAGGAAGTTCTGGAGGGGTTGAAGGGTCCAACTTGATGTCGTCTT

       GCCTTTAGAAAGGGCAGGAGGCCGGCTCTCGAGGTCCTCACCTGAAGTGAGCATGCCAGC
  1741 ---------+---------+---------+---------+---------+---------+ 1800
       CGGAAATCTTTCCCGTCCTCCGGCCGAGAGCTCCAGGAGTGGACTTCACTCGTACGGTCG

       CACTGCAGGAACGCCCCGGGACAGGAATGCCCATTTGTGCAACGAACCCTGACTCCTTCC
  1801 ---------+---------+---------+---------+---------+---------+ 1860
       GTGACGTCCTTGCGGGGCCCTGTCCTTACGGGTAAACACGTTGCTTGGGACTGAGGAAGG

       TCACCCTGACTTCTCCCCCTCCCTACCCGCGCGCAGGCCAAGTTGCTGAATCAATGGAGC
  1861 ---------+---------+---------+---------+---------+---------+ 1920
       AGTGGGACTGAAGAGGGGGAGGGATGGGCGCGCGTCCGGTTCAACGACTTAGTTACCTCG
```

Fig. 8B

```
     CCTCCCCAACCCGGGCGTTCCCCAGCGAGGCTTCCTTCCCATCCTCCTGACCACCGGGGC
1921 ---------+---------+---------+---------+---------+---------+ 1980
     GGAGGGGTTGGGCCCGCAAGGGGTCGCTCCGAAGGAAGGGTAGGAGGACTGGTGGCCCCG

     TTTTCGTGAGCTCGTCTCTGATCTCGCGCAAGAGTGACACACAGGTGTTCAAAGACGCTT
1981 ---------+---------+---------+---------+---------+---------+ 2040
     AAAAGCACTCGAGCAGAGACTAGAGCGCGTTCTCACTGTGTGTCCACAAGTTTCTGCGAA

     CTGGGGAGTGAGGGAAGCGGTTTACGAGTGACTTGGCTGGAGCCTCAGGGGCGGGCACTG
2041 ---------+---------+---------+---------+---------+---------+ 2100
     GACCCCTCACTCCCTTCGCCAAATGCTCACTGAACCGACCTCGGAGTCCCCGCCCGTGAC

     GCACGGAACACACCCTGAGGCCAGCCCTGGCTGCCCAGGCGGAGCTGCCTCTTCTCCCGC
2101 ---------+---------+---------+---------+---------+---------+ 2160
     CGTGCCTTGTGTGGGACTCCGGTCGGGACCGACGGGTCCGCCTCGACGGAGAAGAGGGCG

     GGACATGTACAGAGCTCGAGAAGTACTAGTGGCCACGTGGGCCGTGCACCTTAAGCTTTA
2161 ---------+---------+---------+---------+---------+---------+ 2220
     CCTGTACATGTCTCGAGCTCTTCATGATCACCGGTGCACCCGGCACGTGGAATTCGAAAT

                                                  <---4.p53-BE-
                                                     (intron)
     GGGTCGCTGGAGGGGGACCCCGGTTGGAGAGAGGAGCGGAACTCCTGGACAAGCCCTGAC
2221 ---------+---------+---------+---------+---------+---------+ 2280
     CCCAGCGACCTCCCCCTGGGGCCAACCTCTCTCCTCGCCTTGAGGACCTGTTCGGGACTG

     ---->
     AAGCCAAGCCAAAGGTCCGCTCCGGCGCGGGTGGGTGAGTGCGCGCCGCCCCGCGGGGGC
2281 ---------+---------+---------+---------+---------+---------+ 2340
     TTCGGTTCGGTTTCCAGGCGAGGCCGCGCCCACCCACTCACGCGCGGCGGGGCGCCCCCG

     GGGGAGAGAGCCTGCAGCCTTCAGAACAGATATTGCTCATTTTCTGGCAGTTCTCAGACG
2341 ---------+---------+---------+---------+---------+---------+ 2400
     CCCCTCTCTCGGACGTCGGAAGTCTTGTCTATAACGAGTAAAAGACCGTCAAGAGTCTGC

     TAGGAAATAAGTCAGCACCGAAGCAGTGGTTAAGCCGGAGGGCTCGGAAGAACGGCACCT
2401 ---------+---------+---------+---------+---------+---------+ 2460
     ATCCTTTATTCAGTCGTGGCTTCGTCACCAATTCGGCCTCCCGAGCCTTCTTGCCGTGGA

     TTTCTTTCTCGAAAAAGTTATATGGGGGCTGAATGAGCTTCTGGAGGCTTGTTTACCGTT
2461 ---------+---------+---------+---------+---------+---------+ 2520
     AAAGAAAGAGCTTTTTCAATATACCCCCGACTTACTCGAAGACCTCCGAACAAATGGCAA

     TTTTATTGTCACACAGAAAAGGAAACTGCCTTGTCTCCCTTCCGGGAATTCTCTCTTTAA
2521 ---------+---------+---------+---------+---------+---------+ 2580
     AAAATAACAGTGTGTCTTTTCCTTTGACGGAACAGAGGGAAGGCCCTTAAGAGAGAAATT

     GACTGTAAGTCGCTGCCTGAGTGGTTTCATTTTGTTTTGTTTTTCTGCCCTTCTCTTTCT
2581 ---------+---------+---------+---------+---------+---------+ 2640
     CTGACATTCAGCGACGGACTCACCAAAGTAAAACAAAACAAAAAGACGGGAAGAGAAAGA

     TCTTTTGCCCTTTCTTAGCTTGCACTCCCATGGTGATTTCTGCTTGGTCTCCTGCTGGGG
2641 ---------+---------+---------+---------+---------+---------+ 2700
     AGAAAACGGGAAAGAATCGAACGTGAGGGTACCACTAAAGACGAACCAGAGGACGACCCC
```

Fig. 8C

```
     TTGGTGGTACTCGTTCCCACCGCACAGAACCCGGCGCCTATTATTGGCCAAGAAACTTGA
2701 ---------+---------+---------+---------+---------+---------+ 2760
     AACCACCATGAGCAAGGGTGGCGTGTCTTGGGCCGCGGATAATAACCGGTTCTTTGAACT

     GCAGCCTGTTTTGAAAAGTCCCTCGCTCAGAAATGCCAGCTTGCAGATGGCTAATCAAAG
2761 ---------+---------+---------+---------+---------+---------+ 2820
     CGTCGGACAAAACTTTTCAGGGAGCGAGTCTTTACGGTCGAACGTCTACCGATTAGTTTC

     AGACGTG
2821 ------- 2827
     TCTGCAC
```

Fig. 8D

```
                                                        <---- 1.p53-BE --

    TGAGGACTCTCAGGAATATGCTGGTAAAATAAAAATAACCTTTAGAGATGCCCAAACTGT
  1 ---------+---------+---------+---------+---------+---------+ 60
    ACTCCTGAGAGTCCTTATACGACCATTTTATTTTTATTGGAAATCTCTACGGGTTTGACA

    -->

    TTTCCCCAGAACACCAGCATTCATTAGGTGTTCATTCAATAGATTCTTCAAAGGATTCCA
 61 ---------+---------+---------+---------+---------+---------+ 120
    AAAGGGGTCTTGTGGTCGTAAGTAATCCACAAGTAAGTTATCTAAGAAGTTTCCTAAGGT

    AAGGCAAAGAAGTTTGGGGAACAGTATATATAATTACCCAACCCTTTGACATTAGCATAC
121 ---------+---------+---------+---------+---------+---------+ 180
    TTCCGTTTCTTCAAACCCCTTGTCATATATATTAATGGGTTGGGAAACTGTAATCGTATG

    TAAGGGCCCTGAGAAGTTTTGGATTAAGAAAGTTTTCAAATTAAAGTAACCCAGAATTTT
181 ---------+---------+---------+---------+---------+---------+ 240
    ATTCCCGGGACTCTTCAAAACCTAATTCTTTCAAAAGTTTAATTTCATTGGGTCTTAAAA

    CTAAGATTATTTGACCATGAAACATATGTCTCCCCACAAAGCACATATTCCTATCTCCTT
241 ---------+---------+---------+---------+---------+---------+ 300
    GATTCTAATAAACTGGTACTTTGTATACAGAGGGGTGTTTCGTGTATAAGGATAGAGGAA

    GAACTTGAGGATAATTAGACGTACGTGGGTAGAGGGTAGGGGAAGGGGGTATGGCATAGA
301 ---------+---------+---------+---------+---------+---------+ 360
    CTTGAACTCCTATTAATCTGCATGCACCCATCTCCCATCCCCTTCCCCCATACCGTATCT

    AAGAGCAGGACCTTGGGAGCAAGAATATCTAAGTTTAATTCCTGACTCTGCTATTTATTA
361 ---------+---------+---------+---------+---------+---------+ 420
    TTCTCGTCCTGGAACCCTCGTTCTTATAGATTCAAATTAAGGACTGAGACGATAAATAAT

                    <---- 2.p53-BE ---->

    ACTAACCATCTTTGCCAATGTTGCTTAAGCTTTTTTGGCTACATTTTTTTATTTGTAAAG
421 ---------+---------+---------+---------+---------+---------+ 480
    TGATTGGTAGAAACGGTTACAACGAATTCGAAAAAACCGATGTAAAAAAATAAACATTTC

    TAAGTTTAATAATCACTCATCTCACTGGGCTATAATGATAAGTATTAAGTAAGGAAGATC
481 ---------+---------+---------+---------+---------+---------+ 540
    ATTCAAATTATTAGTGAGTAGAGTGACCCGATATTACTATTCATAATTCATTCCTTCTAG

    CACATATGTGAGTTGCTGGCTTATAATTCACACTCAAGAGATACTGATTTTGTCAATTGT
541 ---------+---------+---------+---------+---------+---------+ 600
    GTGTATACACTCAACGACCGAATATTAAGTGTGAGTTCTCTATGACTAAAACAGTTAACA

    CCTTTCCCCTTTTTTTCTCTCTTCCCTCCTTCCATTCCTTCTTCCCTTACCTCTCCTTTC
601 ---------+---------+---------+---------+---------+---------+ 660
    GGAAAGGGGAAAAAAAGAGAGAAGGGAGGAAGGTAAGGAAGAAGGGAATGGAGAGGAAAG
```

Fig. 9A

```
     CTTCCCTCACACCCCTTTTCCTTCCTTCTTTTTACATTTTTTTATTTAAATGAACTTTTC
 661 ---------+---------+---------+---------+---------+---------+ 720
     GAAGGGAGTGTGGGGAAAAGGAAGGAAGAAAAATGTAAAAAAATAAATTTACTTGAAAAG

     ATTTTGGAATAGTTTTAGGATTTCAAAAAATTTGCAGAGATAATACAGAGAATGCCCATA
 721 ---------+---------+---------+---------+---------+---------+ 780
     TAAAACCTTATCAAAATCCTAAAGTTTTTTAAACGTCTCTATTATGTCTCTTACGGGTAT

     TACCATCCTCCTTATCCCACTTCTTTTTGTGTCTATTAGATGCTCAGAGTGTGTGCACAA
 781 ---------+---------+---------+---------+---------+---------+ 840
     ATGGTAGGAGGAATAGGGTGAAGAAAAACACAGATAATCTACGAGTCTCACACACGTGTT

     GGCTGGCACGCCCAGGGTCTTCCTCATGGCACTAACAGTCTACTGAAAGGTGGAACAGAG
 841 ---------+---------+---------+---------+---------+---------+ 900
     CCGACCGTGCGGGTCCCAGAAGGAGTACCGTGATTGTCAGATGACTTTCCACCTTGTCTC

     ACAAGCCTATCAACACCTACAAGACTGGTGGTAAGTGCAGTGACAGATGCAAAACACAGG
 901 ---------+---------+---------+---------+---------+---------+ 960
     TGTTCGGATAGTTGTGGATGTTCTGACCACCATTCACGTCACTGTCTACGTTTTGTGTCC

     GTGATGGAAAGCCCTCAGGAGGGTAACCTAACCTAGATTTGAGGGCCCAAACAGGCTCCA
 991 ---------+---------+---------+---------+---------+---------+ 1020
     CACTACCTTTCGGGAGTCCTCCCATTGGATTGGATCTAAACTCCCGGGTTTGTCCGAGGT

     GAAGAAAATGTCAACTGAGAGGAAGCCTGAAGGATGAACAGTGGGCTAAGCAAAGGGTTA
1021 ---------+---------+---------+---------+---------+---------+ 1080
     CTTCTTTTACAGTTGACTCTCCTTCGGACTTCCTACTTGTCACCCGATTCGTTTCCCAAT

     TTAATGTGTTATTAATGGGTTGAATCTAATTGGGAAGGGAGAGAGGTTGCAGAGTGAGGT
1081 ---------+---------+---------+---------+---------+---------+ 1140
     AATTACACAATAATTACCCAACTTAGATTAACCCTTCCCTCTCTCCAACGTCTCACTCCA

     GCAGAGCTTGGTGGACGATGCCAAAGGAATACTGAAACCTTTAGTGTGTCCAGTCTGGAA
1141 ---------+---------+---------+---------+---------+---------+ 1200
     CGTCTCGAACCACCTGCTACGGTTTCCTTATGACTTTGGAAATCACACAGGTCAGACCTT

     CTGCATCCAAATTCAGGTTCAGTAATGATGTCATTATCCAAACATACCTTCTGTAAAATT
1201 ---------+---------+---------+---------+---------+---------+ 1260
     GACGTAGGTTTAAGTCCAAGTCATTACTACAGTAATAGGTTTGTATGGAAGACATTTTAA

           <---- 3.p53-BE ---->

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1261 ---------+---------+---------+---------+---------+---------+ 1320
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     TCACCAGAGCACGAAAGAATTACAAGATTTTTTTTAAAGAAAATTGGCCAGGAAATAAT
1321 ---------+---------+---------+---------+---------+---------+ 1380
     AGTGGTCTCGTGCTTTCTTAATGTTCTAAAAAAAAATTTCTTTTAACCGGTCCTTTATTA

     GAGTAACGAAGGACAGGAAGTAATTGTGAATGTTTAATATAGCTGGGGCTATGCGATTTG
1381 ---------+---------+---------+---------+---------+---------+ 1440
     CTCATTGCTTCCTGTCCTTCATTAACACTTACAAATTATATCGACCCCGATACGCTAAAC

     GCTTAAGTTGTTAGCTTTGTTTTCCTCTTGAGAAATAAAAACTAAGGGGCCCTCCCTTTT
1441 ---------+---------+---------+---------+---------+---------+ 1500
     CGAATTCAACAATCGAAACAAAAGGAGAACTCTTTATTTTTGATTCCCCGGGAGGGAAAA

     CAGAGCCCTATGGCGCAACATCTGTACTTTTTCATATGGTTAACTGTCCATTCCAGGAAC
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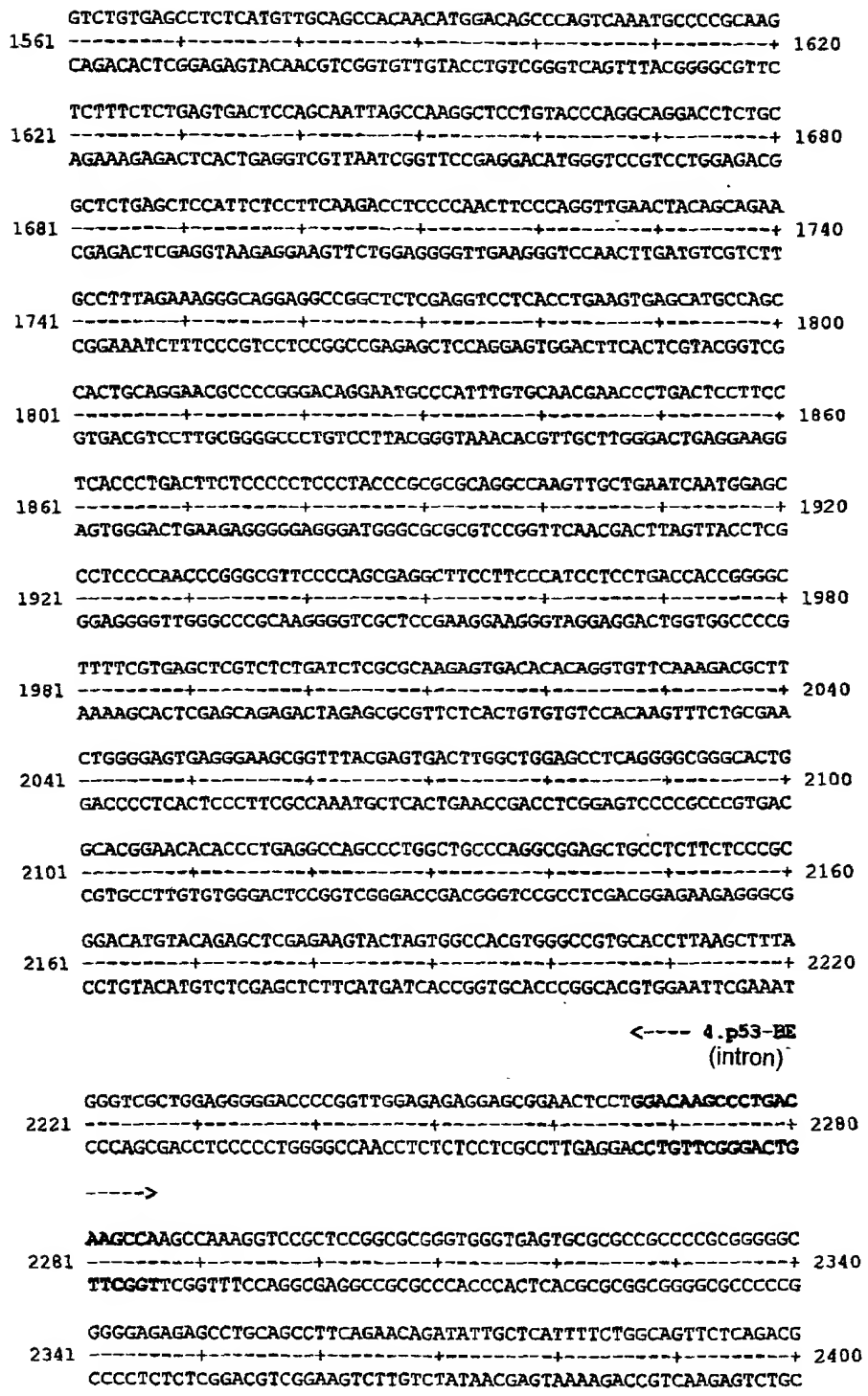
Fig. 9B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1620
TCTTTCTCTGAGTGACTCCAGCAATTAGCCAAGGCTCCTGTACCCAGGCAGGACCTCTGC
1621
AGAAAGAGACTCACTGAGGTCGTTAATCGGTTCCGAGGACATGGGTCCGTCCTGGAGACG
1680
GCTCTGAGCTCCATTCTCCTTCAAGACCTCCCCAACTTCCCAGGTTGAACTACAGCAGAA
1681
CGAGACTCGAGGTAAGAGGAAGTTCTGGAGGGGTTGAAGGGTCCAACTTGATGTCGTCTT
1740
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1741
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1800
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1860
TCACCCTGACTTCTCCCCCTCCCTACCCGCGCGCAGGCCAAGTTGCTGAATCAATGGAGC
1861
AGTGGGACTGAAGAGGGGGAGGGATGGGCGCGCGTCCGGTTCAACGACTTAGTTACCTCG
1920
CCTCCCCAACCCGGGCGTTCCCCAGCGAGGCTTCCTTCCCATCCTCCTGACCACCGGGGC
1921
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1980
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1981
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2041
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2100
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2101
CGTGCCTTGTGTGGGACTCCGGTCGGGACCGACGGGTCCGCCTCGACGGAGAAGAGGGCG
2160
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2161
CCTGTACATGTCTCGAGCTCTTCATGATCACCGGTGCACCCGGCACGTGGAATTCGAAAT
2220
<---- 4.p53-BE
(intron)
GGGTCGCTGGAGGGGGACCCCGGTTGGAGAGAGGAGCGGAACTCCTGGACAAGCCCTGAC
2221
CCCAGCGACCTCCCCCTGGGGCCAACCTCTCTCCTCGCCTTGAGGACCTGTTCGGGACTG
2280
----->
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2281
TTCGGTTCGGTTTCCAGGCGAGGCCGCGCCCACCCACTCACGCGCGGCGGGGCGCCCCCG
2340
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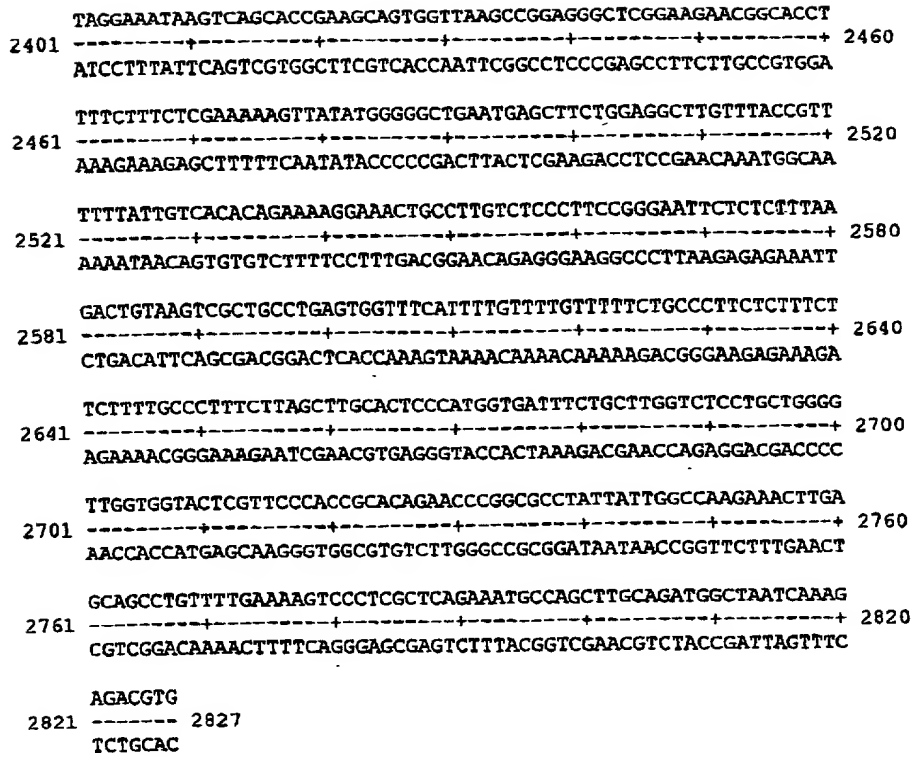
2400

Fig. 9C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TTTCTTTCTCGAAAAAGTTATATGGGGGCTGAATGAGCTTCTGGAGGCTTGTTTACCGTT
2461 ---------+---------+---------+---------+---------+---------+ 2520
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2521 ---------+---------+---------+---------+---------+---------+ 2580
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GACTGTAAGTCGCTGCCTGAGTGGTTTCATTTTGTTTTGTTTTTCTGCCCTTCTCTTTCT
2581 ---------+---------+---------+---------+---------+---------+ 2640
CTGACATTCAGCGACGGACTCACCAAAGTAAAACAAAACAAAAAGACGGGAAGAGAAAGA
TCTTTTGCCCTTTCTTAGCTTGCACTCCCATGGTGATTTCTGCTTGGTCTCCTGCTGGGG
2641 ---------+---------+---------+---------+---------+---------+ 2700
AGAAAACGGGAAAGAATCGAACGTGAGGGTACCACTAAAGACGAACCAGAGGACGACCCC
TTGGTGGTACTCGTTCCCACCGCACAGAACCCGGCGCCTATTATTGGCCAAGAAACTTGA
2701 ---------+---------+---------+---------+---------+---------+ 2760
AACCACCATGAGCAAGGGTGGCGTGTCTTGGGCCGCGGATAATAACCGGTTCTTTGAACT
GCAGCCTGTTTTGAAAAGTCCCTCGCTCAGAAATGCCAGCTTGCAGATGGCTAATCAAAG
2761 ---------+---------+---------+---------+---------+---------+ 2820
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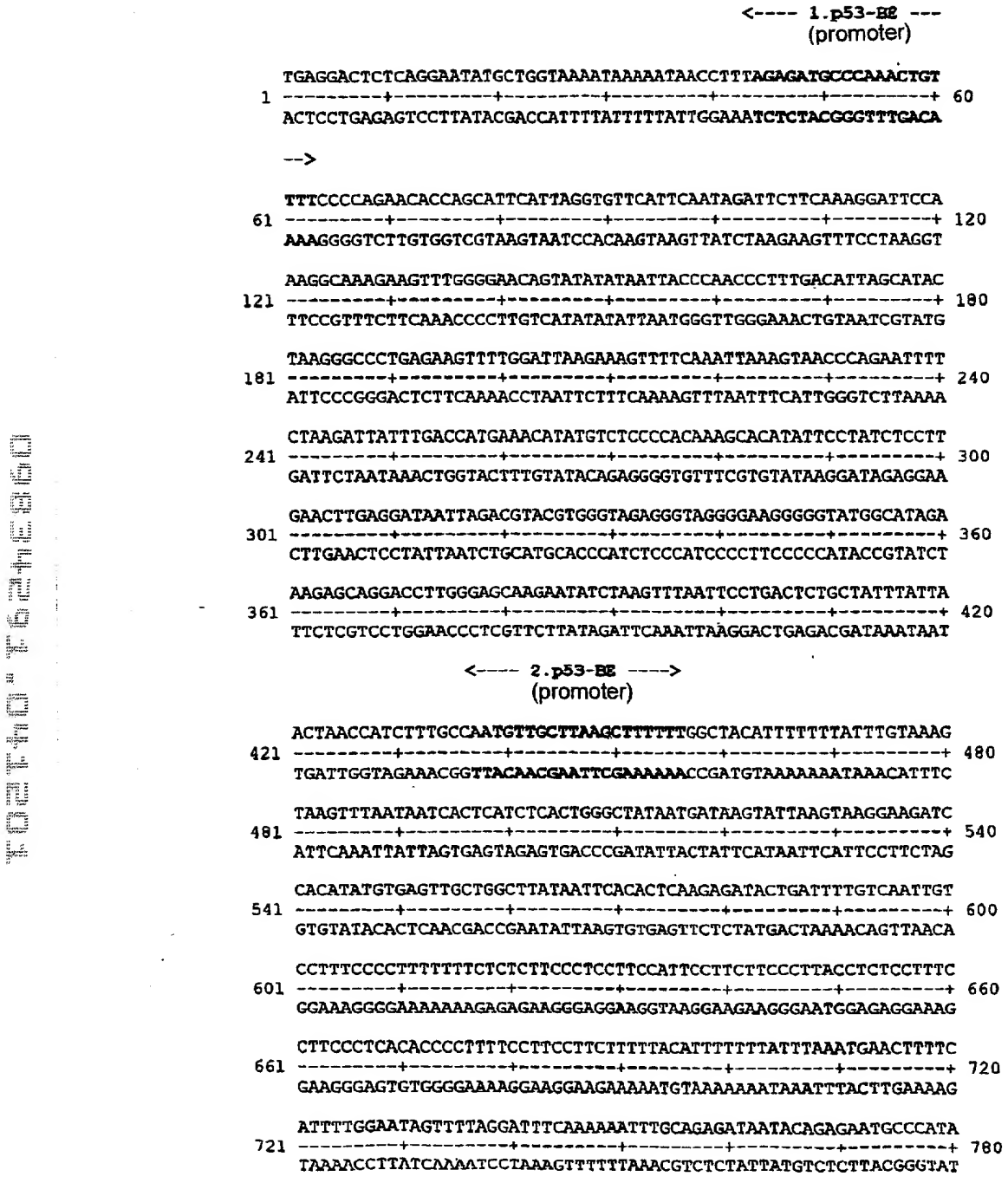
AGACGTG
2821 ------- 2827
TCTGCAC

Fig. 9D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61
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121
TTCCGTTTCTTCAAACCCCTTGTCATATATATTAATGGGTTGGGAAACTGTAATCGTATG
TAAGGGCCCTGAGAAGTTTTGGATTAAGAAAGTTTTCAAATTAAAGTAACCCAGAATTTT
181
ATTCCCGGGACTCTTCAAAACCTAATTCTTTCAAAAGTTTAATTTCATTGGGTCTTAAAA
CTAAGATTATTTGACCATGAAACATATGTCTCCCCACAAAGCACATATTCCTATCTCCTT
241
GATTCTAATAAACTGGTACTTTGTATACAGAGGGGTGTTTCGTGTATAAGGATAGAGGAA
GAACTTGAGGATAATTAGACGTACGTGGGTAGAGGGTAGGGGAAGGGGGTATGGCATAGA
301
CTTGAACTCCTATTAATCTGCATGCACCCATCTCCCATCCCCTTCCCCCATACCGTATCT
AAGAGCAGGACCTTGGGAGCAAGAATATCTAAGTTTAATTCCTGACTCTGCTATTTATTA
361
TTCTCGTCCTGGAACCCTCGTTCTTATAGATTCAAATTAAGGACTGAGACGATAAATAAT
<---- 2.p53-BE ---->
(promoter)
ACTAACCATCTTTGCCAATGTTGCTTAAGCTTTTTTGGCTACATTTTTTTATTTGTAAAG
421
TGATTGGTAGAAACGGTTACAACGAATTCGAAAAAACCGATGTAAAAAAATAAACATTTC
TAAGTTTAATAATCACTCATCTCACTGGGCTATAATGATAAGTATTAAGTAAGGAAGATC
481
ATTCAAATTATTAGTGAGTAGAGTGACCCGATATTACTATTCATAATTCATTCCTTCTAG
CACATATGTGAGTTGCTGGCTTATAATTCACACTCAAGAGATACTGATTTTGTCAATTGT
541
GTGTATACACTCAACGACCGAATATTAAGTGTGAGTTCTCTATGACTAAAACAGTTAACA
CCTTTCCCCTTTTTTTCTCTCTTCCCTCCTTCCATTCCTTCTTCCCTTACCTCTCCTTTC
601
GGAAAGGGGAAAAAAAGAGAGAAGGGAGGAAGGTAAGGAAGAAGGGAATGGAGAGGAAAG
CTTCCCTCACACCCCTTTTCCTTCCTTCTTTTTACATTTTTTTATTTAAATGAACTTTTC
661
GAAGGGAGTGTGGGGAAAAGGAAGGAAGAAAAATGTAAAAAAATAAATTTACTTGAAAAG
ATTTTGGAATAGTTTTAGGATTTCAAAAAATTTGCAGAGATAATACAGAGAATGCCCATA
721
TAAAACCTTATCAAAATCCTAAAGTTTTTTAAACGTCTCTATTATGTCTCTTACGGGTAT

Fig. 10A

```
      TACCATCCTCCTTATCCCACTTCTTTTTGTGTCTATTAGATGCTCAGAGTGTGTGCACAA
 781  ---------+---------+---------+---------+---------+---------+ 840
      ATGGTAGGAGGAATAGGGTGAAGAAAAACACAGATAATCTACGAGTCTCACACACGTGTT

      GGCTGGCACGCCCAGGGTCTTCCTCATGGCACTAACAGTCTACTGAAAGGTGGAACAGAG
 841  ---------+---------+---------+---------+---------+---------+ 900
      CCGACCGTGCGGGTCCCAGAAGGAGTACCGTGATTGTCAGATGACTTTCCACCTTGTCTC

      ACAAGCCTATCAACACCTACAAGACTGGTGGTAAGTGCAGTGACAGATGCAAAACACAGG
 901  ---------+---------+---------+---------+---------+---------+ 960
      TGTTCGGATAGTTGTGGATGTTCTGACCACCATTCACGTCACTGTCTACGTTTTGTGTCC

      GTGATGGAAAGCCCTCAGGAGGGTAACCTAACCTAGATTTGAGGGCCCAACAGGCTCCAG
 961  ---------+---------+---------+---------+---------+---------+ 1020
      CACTACCTTTCGGGAGTCCTCCCATTGGATTGGATCTAAACTCCCGGGTTGTCCGAGGTC

      AAGAAAATGTCAACTGAGAGGAAGCCTGAAGGATGAACAGTGGGCTAAGCAAAGGGTTAT
1021  ---------+---------+---------+---------+---------+---------+ 1080
      TTCTTTTACAGTTGACTCTCCTTCGGACTTCCTACTTGTCACCCGATTCGTTTCCCAATA

      TAATGTGTTATTAATGGGTTGAATCTAATTGGGAAGGGAGAGAGGTTGCAGAGTGAGGTG
1081  ---------+---------+---------+---------+---------+---------+ 1140
      ATTACACAATAATTACCCAACTTAGATTAACCCTTCCCTCTCTCCAACGTCTCACTCCAC

      CAGAGCTTGGTGGACGATGCCAAAGGAATACTGAAACCTTTAGTGTGTCCAGTCTGGAAC
1141  ---------+---------+---------+---------+---------+---------+ 1200
      GTCTCGAACCACCTGCTACGGTTTCCTTATGACTTTGGAAATCACACAGGTCAGACCTTG

      TGCATCCAAATTCAGGTTCAGTAATGATGTCATTATCCAAACATACCTTCTGTAAAATTC
1201  ---------+---------+---------+---------+---------+---------+ 1260
      ACGTAGGTTTAAGTCCAAGTCATTACTACAGTAATAGGTTTGTATGGAAGACATTTTAAG

          <---- 3.p53-BE ---->
               (promoter)
      ATGCTAAACTACCTAAGAGCTATCTACCGTTCCAAAGCAATAGTGACTTTGAACAGTGTT
1261  ---------+---------+---------+---------+---------+---------+ 1320
      TACGATTTGATGGATTCTCGATAGATGGCAAGGTTTCGTTATCACTGAAACTTGTCACAA

      CACCAGAGCACGAAAGAATTACAAGATTTTTTTTAAAGAAAATTGGCCAGGAAATAATG
1321  ---------+---------+---------+---------+---------+---------+ 1380
      GTGGTCTCGTGCTTTCTTAATGTTCTAAAAAAAATTTCTTTTAACCGGTCCTTTATTAC

      AGTAACGAAGGACAGGAAGTAATTGTGAATGTTTAATATAGCTGGGGCTATGCGATTTGG
1381  ---------+---------+---------+---------+---------+---------+ 1440
      TCATTGCTTCCTGTCCTTCATTAACACTTACAAATTATATCGACCCCGATACGCTAAACC

      CTTAAGTTGTTAGCTTTGTTTTCCTCTTGAGAAATAAAAACTAAGGGGCCCTCCCTTTTC
1441  ---------+---------+---------+---------+---------+---------+ 1500
      GAATTCAACAATCGAAACAAAAGGAGAACTCTTTATTTTTGATTCCCCGGGAGGGAAAAG

      AGAGCCTTATGGCGCAACATCTGTACTTTTTCATATGGTTAACTGTCCATTCCAGAAACG
1501  ---------+---------+---------+---------+---------+---------+ 1560
      TCTCGGAATACCGCGTTGTAGACATGAAAAAGTATACCAATTGACAGGTAAGGTCTTTGC

      TCTGTGAGCCTCTCATGTTGCAGCCACAACATGGACAGCCCAGTCAAATGCCCCGCAAGT
1561  ---------+---------+---------+---------+---------+---------+ 1620
      AGACACTCGGAGAGTACAACGTCGGTGTTGTACCTGTCGGGTCAGTTTACGGGGCGTTCA

      CTTTCTCTGAGTGACTCCAGCAATTAGCCAAGGCTCCTGTACCCAGGCAGGACCTCTGCG
1621  ---------+---------+---------+---------+---------+---------+ 1680
      GAAAGAGACTCACTGAGGTCGTTAATCGGTTCCGAGGACATGGGTCCGTCCTGGAGACGC

      CTCTGAGCTCCATTCTCCTTCAAGACCTCCCCAACTTCCCAGGTTGAACTACAGCAGAAG
1681  ---------+---------+---------+---------+---------+---------+ 1740
      GAGACTCGAGGTAAGAGGAAGTTCTGGAGGGGTTGAAGGGTCCAACTTGATGTCGTCTTC
```

Fig. 10B

```
     CCTTTAGAAAGGGCAGGAGGCCGGCTCTCGAGGTCCTCACCTGAAGTGAGCATGCCAGCC
1741 ---------+---------+---------+---------+---------+---------+ 1800
     GGAAATCTTTCCCGTCCTCCGGCCGAGAGCTCCAGGAGTGGACTTCACTCGTACGGTCGG

     ACTGCAGGAACGCCCCGGGACAGGAATGCCCATTTGTGCAACGAACCCTGACTCCTTCCT
1801 ---------+---------+---------+---------+---------+---------+ 1860
     TGACGTCCTTGCGGGGCCCTGTCCTTACGGGTAAACACGTTGCTTGGGACTGAGGAAGGA

     CACCCTGACTTCTCCCCCTCCCTACCCGCGCGCAGGCCAAGTTGCTGAATCAATGGAGCC
1861 ---------+---------+---------+---------+---------+---------+ 1920
     GTGGGACTGAAGAGGGGGAGGGATGGGCGCGCGTCCGGTTCAACGACTTAGTTACCTCGG

     CTCCCCAACCCGGGCGTTCCCCAGCGAGGCTTCCTTCCCATCCTCCTGACCACCGGGGCT
1921 ---------+---------+---------+---------+---------+---------+ 1980
     GAGGGGTTGGGCCCGCAAGGGGTCGCTCCGAAGGAAGGGTAGGAGGACTGGTGGCCCCGA

     TTTCGTGAGCTCGTCTCTGATCTCGCGCAAGAGTGACACACAGGTGTTCAAAGACGCTTC
1981 ---------+---------+---------+---------+---------+---------+ 2040
     AAAGCACTCGAGCAGAGACTAGAGCGCGTTCTCACTGTGTGTCCACAAGTTTCTGCGAAG

     TGGGGAGTGAGGGAAGCGGTTTACGAGTGACTTGGCTGGAGCCTCAGGGGCGGGCACTGG
2041 ---------+---------+---------+---------+---------+---------+ 2100
     ACCCCTCACTCCCTTCGCCAAATGCTCACTGAACCGACCTCGGAGTCCCCGCCCGTGACC

     CACGGAACACACCCTGAGGCCAGCCCTGGCTGCCCAGGCGGAGCTGCCTCTTCTCCCGCG
2101 ---------+---------+---------+---------+---------+---------+ 2160
     GTGCCTTGTGTGGGACTCCGGTCGGGACCGACGGGTCCGCCTCGACGGAGAAGAGGGCGC

     GGTTGGTGGACCCGCTCAGTACGGAGTTGGGGAAGCTCTTTCACTTCGGAGGATTGCTCA
2161 ---------+---------+---------+---------+---------+---------+ 2220
     CCAACCACCTGGGCGAGTCATGCCTCAACCCCTTCGAGAAAGTGAAGCCTCCTAACGAGT

     ACAACCATGCTGGGCATCTGGACCCTCCTACCTCTGGTGATCCCTCTCCTGCCCGGGTGG
2221 ---------+---------+---------+---------+---------+---------+ 2280
     TGTTGGTACGACCCGTAGACCTGGGAGGATGGAGACCACTAGGGAGAGGACGGGCCCACC

     AGGCTTACCCCGTCTTAGTCCCGGGGATAGGCAAAGTGGGGCGGGCGCGGGACGCGTGCG
2281 ---------+---------+---------+---------+---------+---------+ 2340
     TCCGAATGGGGCAGAATCAGGGCCCCTATCCGTTTCACCCCGCCCGCGCCCTGCGCACGC

     GGATTGCGGCGGCAGCGGCGCACGCGGGCACCTGGGAGCGGCGGGCTGCTGCGGGAGGCG
2341 ---------+---------+---------+---------+---------+---------+ 2400
     CCTAACGCCGCCGTCGCCGCGTGCGCCCGTGGACCCTCGCCGCCCGACGACGCCCTCCGC

     TTGGAGACTGGCTCCCGGGGGCTGTTAGGACCTTCCCTCAGGCCCGGGTGCTCAGAACGA
2401 ---------+---------+---------+---------+---------+---------+ 2460
     AACCTCTGACCGAGGGCCCCCGACAATCCTGGAAGGGAGTCCGGGCCCACGAGTCTTGCT

     TGGAGGACTTGCTTTTCTTGGGCCTTGATGCGAAGTGCTGATCCCGCTGGGCAGGCGGGG
2461 ---------+---------+---------+---------+---------+---------+ 2520
     ACCTCCTGAACGAAAAGAACCCGGAACTACGCTTCACGACTAGGGCGACCCGTCCGCCCC

     CAGCTCCGGCGCTCCTCGGAGACCACTGCGCTCCACGTTGAGGTGGGCGTGGGGGGCGGA
2521 ---------+---------+---------+---------+---------+---------+ 2580
     GTCGAGGCCGCGAGGAGCCTCTGGTGACGCGAGGTGCAACTCCACCCGCACCCCCCGCCT

     CAGGAATTGAAGCGGAAGTCTGGGAAGCTTTAGGGTCGCTGGAGGGGGACCCCGGTTGGA
2581 ---------+---------+---------+---------+---------+---------+ 2640
     GTCCTTAACTTCGCCTTCAGACCCTTCGAAATCCCAGCGACCTCCCCCTGGGGCCAACCT

                          <---- 4.p53-BE ---->
                               (intron)

     GAGAGGAGCGGAACTCCTGGACAAGCCCTGACAAGCCAAGCCAAAGGTCCGCTCCGGCGC
2641 ---------+---------+---------+---------+---------+---------+ 2700
     CTCTCCTCGCCTTGAGGACCTGTTCGGGACTGTTCGGTTCGGTTTCCAGGCGAGGCCGCG
```

Fig. 10C

```
     GGGTGGGTGAGTGCGCGCCGCCCCGCGGGGGCGGGGAGAGAGCCTACAGCCTTCAGAACA
2701 ---------+---------+---------+---------+---------+---------+ 2760
     CCCACCCACTCACGCGCGGCGGGGCGCCCCCGCCCCTCTCTCGGATGTCGGAAGTCTTGT

     CATATTGCTCATTTTCTGGCAGTTCTCAGACGTAGGAAATAAGTCAGCACCGAAGCAGTG
2761 ---------+---------+---------+---------+---------+---------+ 2820
     GTATAACGAGTAAAAGACCGTCAAGAGTCTGCATCCTTTATTCAGTCGTGGCTTCGTCAC

     GTTAAGCCGGAGGGCTCGGAAGAACGGCACCTTTTCTTTCTCGAAAAAGTTATATGGGGG
2821 ---------+---------+---------+---------+---------+---------+ 2880
     CAATTCGGCCTCCCGAGCCTTCTTGCCGTGGAAAAGAAAGAGCTTTTTCAATATACCCCC

     CTGAATGAGCTTCTGGAGGCTTGTTTACCGTTTTTTATTGTCACACAGAAAAGGAAACTG
2881 ---------+---------+---------+---------+---------+---------+ 2940
     GACTTACTCGAAGACCTCCGAACAAATGGCAAAAAATAACAGTGTGTCTTTTCCTTTGAC

     CCTTGTCTCCCTTCCGGGAATTCTCTCTTTAAGACTGTAAGTCGCTGCCTGAGTGGTTTC
2941 ---------+---------+---------+---------+---------+---------+ 3000
     GGAACAGAGGGAAGGCCCTTAAGAGAGAAATTCTGACATTCAGCGACGGACTCACCAAAG

     ATTTTGTTTTGTTTTTCTGCCCTTCTCTTTCTTCTTTTGCCCTTTCTTAGCTTGCACTCC
3001 ---------+---------+---------+---------+---------+---------+ 3060
     TAAAACAAAACAAAAAGACGGGAAGAGAAAGAAGAAAACGGGAAAGAATCGAACGTGAGG

     CATGGTGATTTCTGCTTGGTCTCCTGCTGGGGTTGGTGGTACTCGTTCCCACCGCACAGA
3061 ---------+---------+---------+---------+---------+---------+ 3120
     GTACCACTAAAGACGAACCAGAGGACGACCCCAACCACCATGAGCAAGGGTGGCGTGTCT

     ACCCGGCGCCTATTATTGGCCAAGAAACTTGAGCAGCCTGTTTTGAAAAGTCCCTCGCTC
3121 ---------+---------+---------+---------+---------+---------+ 3180
     TGGGCCGCGGATAATAACCGGTTCTTTGAACTCGTCGGACAAAACTTTTCAGGGAGCGAG

     AGAAATGCCAGCTTGCAGATGGCTAATCAAAG
3181 ---------+---------+---------+-- 3212
     TCTTTACGGTCGAACGTCTACCGATTAGTTTC
```

Fig. 10D

Fig. 11A

variations in the p53 binding region of figure 8

1. **p1140 IMI**

p1140	GGACAAGCCCTGACAAGCCA
p1140 IMI	GGA**A**AAGCCCTGACAAGCCA

positions of the mutations (boldface and arrow): 2270 (C→A)

2. **p1140 IMII**

p1140	GGACAAGCCCTGACAAGCCA
p1140 IMII	GGA**A**AAGCCCTGA**A**AAGCCA

positions of the mutations (boldface and arrow): 2270 (C→A)
2280 (C→A)

3. **p1140 IMIII**

p1140	GGACAAGCCCTGACAAGCCA
p1140 IMIII	GGA**AA**A**T**CCCTGA**A**AA**T**CCA

positions of the mutations (boldface and arrow): 2270 (C→A)
2273 (G→T)
2280 (C→A)
2283 (G→T)

Fig. 11B

4. **p1140 IMIV**

```
p1140          GGACAAGCCCTGACAAGCCA
p1140 IMIV     GCACAAGCCCTCACAAGCCA
                ↑         ↑
```

positions of the mutations (boldface and arrow): 2268 (G→T)
2278 (C→A)

Fig. 12A

variations in the p53 binding regions of figure 9

1. p1141 IMIII

```
p1141          GGACAAGCCCTGACAAGCCA
p1141 IMIII    GGAAAATCCCTGAAAATCCA
                 ↑ ↑     ↑ ↑
```

positions of the mutations (boldface and arrow): **2270**
2273
2280
2283

2. p1141 1p53

```
p1141          AGAGATGCCCAAACTGTTTT
p1141 1p53     AGAGATTCCCAAAATGTTTT
                    ↑       ↑
```

positions of the mutations (boldface and arrow): **50**
57

3. p1141 2p53

```
p1141          AATGTTGCTTAAGCTTTTTT
p1141 2p53     AATGTTTCTTAAGATTTTTT
                    ↑       ↑
```

positions of the mutations (boldface and arrow): **443**
450

Fig. 12B

4. p1141 3p53

```
p1141          AAACTACCTAAGAGCTATCT
p1141 3p53     ACAATACCTAAGAGCTATCT
                ↑ ↑
```

positions of the mutations (boldface and arrow): 1268 (A→C)
1270 (C→A)

5. p1141 ΔBgl

```
                          <---- 1.p53-BE ---->
p1141          AATAACCTTTAGAGATGCCCAAACTGTTTTCCCCAGAACA
p1141ΔBgl      AATAACCTTTA--------------GATCTCCCCAGAACA
```

6. p1141 ΔSpe

```
                          <---- 2.p53-BE ---->
p1141          CATCTTTGCCAATGTTGCTTAAGCTTTTTTGGCTACATTT
p1141ΔBgl      CATCTTTGCCA--------------CTAGTGGCTACATTT
```

7. p1141 ΔMph

```
                          <---- 3.p53-BE ---->
p1141          AATTCATGCTAAACTACCTAAGAGCTATCTACCGTTCCAA
p1141ΔBgl      AATTCATGCTATGCA--------------TACCGTTCCAA
```

Fig. 13A

variations in the p53 binding region of figure 10

1. p1142 TAG

mutation of the positions: 2227 (A→T)
2228 (T→A)

2. p1142 IMIII

p1142 GGACAAGCCCTGACAAGCCA

p1142 IMIII GGA**A**AA**T**CCCTGA**A**AA**T**CCA
↑ ↑ ↑ ↑

positions of the mutations (boldface and arrow): 2662 (C→A)
2665 (G→T)
2672 (C→A)
2675 (G→T)

3. . p1142 ΔBgl

<---- 1.p53-BE ---->
p1142 AATAACCTTT**AGAGATGCCCAAACTGTTTT**CCCCAGAACA
p1142ΔBgl AATAACCTTT**A**----------**GATCT**CCCCAGAACA

4. p1142 ΔSpe

<---- 2.p53-BE ---->
p1142 CATCTTTGCC**AATGTTGCTTAAGCTTTTTT**GGCTACATTT
p1142ΔBgl CATCTTTGCC**A**----------**CTAGT**GGCTACATTT

Fig. 13B

5. p1142 ΔMph

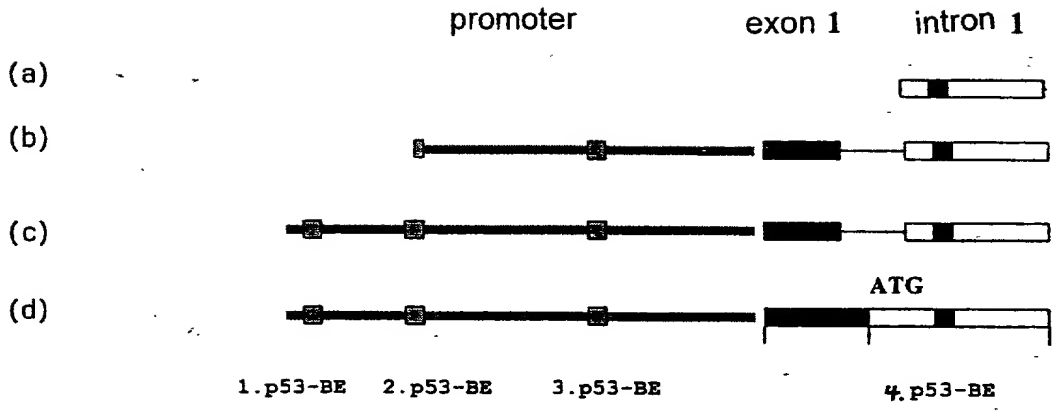
promoter
exon 1
intron 1
(a)
(b)
(c)
(d)
ATG
1.p53-BE
2.p53-BE
3.p53-BE
4.p53-BE

Fig. 14